

WE CLAIM:

1. A method for increasing toughness or stiffness of bone at a site of a potential or actual trauma in a subject in need thereof, comprising administering to
5 the subject an effective amount of a parathyroid hormone.
2. The method of claim 1, wherein the trauma is a potential trauma comprising a fracture, a surgery, or an orthopedic procedure comprising manipulation of a bone at a site of abnormally low bone mass or poor bone structure.
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3. The method of claim 2, wherein the surgery is a joint replacement, a spine bracing, or a combination thereof.
4. The method of claim 3, wherein the joint replacement comprises hip
15 replacement.
5. The method of claim 2, wherein the fracture comprises a vertebral fracture, a non-vertebral fracture, or a combination thereof.
- 20 6. The method of claim 6, wherein the non-vertebral fracture comprises a hip fracture, a fracture of a distal forearm, a fracture of a proximal humerus, a fracture of a wrist, a fracture of a radius, a fracture of an ankle, a fracture of an humerus, a fracture of a rib, a fracture of a foot, a fracture of a pelvis, or a combination thereof.
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7. The method of claim 1, wherein the trauma is a potential trauma comprising trauma related to hypoparathyroidism or to progression of kyphosis.
8. The method of claim 1, wherein the trauma is an actual trauma
30 comprising a fracture.

9. The method of claim 8, wherein the fracture comprises a vertebral fracture, a non-vertebral fracture, or a combination thereof.

10. The method of claim 9, wherein the non-vertebral fracture comprises
5 a hip fracture, a fracture of a distal forearm, a fracture of a proximal humerus, a fracture of a wrist, a fracture of a radius, a fracture of an ankle, a fracture of an humerus, a fracture of a rib, a fracture of a foot, a fracture of a pelvis, or a combination thereof.

10 11. The method of claim 1, wherein the bone comprises an immobilized bone or skeleton, a bone or skeleton deficient in mineral, or a combination thereof.

12. The method of claim 1, wherein the bone comprises cortical bone, cancellous bone, trabecular bone, or a combination thereof.

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13. The method of claim 12, wherein the bone comprises a site of attachment for a ligament, a tendon, a muscle, or a combination thereof.

14. The method of claim 1, wherein the trauma site is a hip, a spine, or a
20 combination thereof.

15. The method of claim 14, wherein the trauma site comprises a femur neck, a trochantera of a femur, an ilium, or a combination thereof.

25 16. The method of claim 15, wherein the trauma site comprises cancellous bone of the ilium.

17. The method of claim 14, wherein the trauma site comprises a mid-thoracic vertebra, an upper lumbar vertebra, or a combination thereof.

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18. The method of claim 1, wherein the subject is a woman at risk for osteoporosis.

19. The method of claim 18, wherein the subject is a postmenopausal
5 woman.

20. The method of claim 19, wherein the woman is independent of hormone replacement therapy or an antiresorptive.

10 21. The method of claim 1, wherein the subject is a woman in an early stage of osteoporosis or in an advanced stage of osteoporosis.

22. The method of claim 1, wherein increasing toughness or stiffness comprises increasing toughness and stiffness.

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23. The method of claim 1, wherein increasing toughness or stiffness comprises decreasing risk or probability of fracture.

24. The method of claim 1, wherein increasing toughness or stiffness
20 comprises increasing activation frequency or bone formation rate in cortical and trabecular bone.

25. The method of claim 1, wherein increasing toughness or stiffness comprises increasing bone mineral content, increasing bone mineral density,
25 increasing trabecular number, increasing trabecular thickness, reducing marrow space, increasing trabecular connectivity, increasing connectivity, increasing resistance to loading, increasing periosteal and endocortical bone formation, increasing cortical porosity, increasing cross sectional bone area and bone mass, increasing work to failure, decreasing elastic modulus, or a combination thereof.

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26. The method of claim 1, wherein administering comprises subcutaneous administration.

27. The method of claim 1, wherein the parathyroid hormone is
5 administered cyclically or intermittently.

28. The method of claim 27, wherein cyclic administration comprises administering the parathyroid hormone for at least 2 remodeling cycles and withdrawing parathyroid hormone for at least 1 remodeling cycle.
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29. The method of claim 27, wherein cyclic administration comprises administering the parathyroid hormone for at least about 12 to about 24 months and withdrawing parathyroid hormone for at least 6 months.

15 30. The method of claim 1, wherein the parathyroid hormone is a fragmented hormone selected from the group consisting of PTH(1-31), PTH(1-34), PTH(1-37), PTH(1-38), and PTH(1-41).

31. The method of claim 1, wherein the parathyroid hormone is human
20 PTH(1-34).

32. The method of claim 1, wherein the parathyroid hormone is human PTH(1-84).

25 33. The method of claim 1, wherein the parathyroid hormone is administered at a dose of at least about 5 $\mu\text{g/kg/day}$.

34. The method of claim 33, wherein the dose is about 10 to about 40 $\mu\text{g/kg/day}$.
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35. The method of claim 1, further comprising administering calcium, vitamin D, or a combination thereof.

36. The method of claim 1, wherein increasing toughness or stiffness
5 comprises increasing bone mineral content of medium density bone.

37. The method of claim 1, wherein increasing toughness or stiffness comprises increasing bone mineral content of low and high density bone and reduction of bone mineral content of medium density bone.

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38. The method of claim 1, wherein increasing toughness or stiffness comprises increasing bone mineral content of medium density bone followed by increasing bone mineral content of low and high density bone and reduction of bone mineral content of medium density bone.

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39. The method of claim 1, wherein increasing toughness or stiffness comprises reducing the size of crystallites in the bone.

40. The method of claim 39, further comprising maturing crystallites of
20 the bone.

41. The method of claim 1, wherein increasing toughness or stiffness comprises increasing mineralization of the bone.

25 42. The method of claim 1, wherein increasing toughness or stiffness comprises reducing incidence of fracture.

43. The method of claim 42, wherein increasing toughness or stiffness comprises reducing incidence of vertebral fracture, reducing incidence of severe
30 fracture, reducing incidence of moderate fracture, reducing incidence of non-vertebral fracture, reducing incidence of multiple fracture, or a combination thereof.

44. A method for reducing the risk of bone fracture in a subject in need thereof, comprising administering to the subject an effective amount of a parathyroid hormone.

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45. The method of claim 44, wherein the bone comprises a hip, a radius, an ankle, an humerus, a rib, a foot, a pelvis, a spine or a combination thereof.

46. The method of claim 44, wherein the parathyroid hormone is a
10 fragmented hormone selected from the group consisting of PTH(1-31), PTH(1-34), PTH(1-37), PTH(1-38), and PTH(1-41).

47. The method of claim 44, wherein the fracture comprises a vertebral fracture, a non-vertebral fracture, or a combination thereof.

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48. The method of claim 47, wherein the non-vertebral fracture comprises a hip fracture, a fracture of a distal forearm, a fracture of a proximal humerus, a fracture of a wrist, a fracture of a radius, a fracture of an ankle, a fracture of an humerus, a fracture of a rib, a fracture of a foot, a fracture of a pelvis, or a
20 combination thereof.

49. A process for manufacturing a medicament used for increasing toughness or stiffness of bone at a site of potential or actual trauma, comprising combining a parathyroid hormone with a pharmaceutically acceptable carrier.

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50. The process of claim 49, wherein the medicament comprises a stabilized formulation of a parathyroid hormone.

51. The process of claim 50, wherein the stabilized formulation
30 comprises:

a therapeutically effective amount of parathyroid hormone;

a polyol, such as mannitol or propylene glycol;
a buffering agent suitable for maintaining the pH of the composition within a range of about 3-7, such as an acetate or tartrate source; and
water.

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52. The use of a parathyroid hormone in the manufacture of a medicament for reducing the risk of bone fracture in a subject in need thereof.

53. The method of claim 52, wherein the bone comprises a hip, a radius,
10 an ankle, an humerus, a rib, a foot, a pelvis, a spine or a combination thereof.

54. The method of claim 52, wherein the parathyroid hormone is a fragmented hormone selected from the group consisting of PTH(1-31), PTH(1-34), PTH(1-37), PTH(1-38), and PTH(1-41).

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55. The method of claim 52, wherein the fracture comprises a vertebral fracture, a non-vertebral fracture, or a combination thereof.

56. The method of claim 55, wherein the non-vertebral fracture
20 comprises a hip fracture, a fracture of a distal forearm, a fracture of a proximal humerus, a fracture of a wrist, a fracture of a radius, a fracture of an ankle, a fracture of an humerus, a fracture of a rib, a fracture of a foot, a fracture of a pelvis, or a combination thereof.

25 57. The use of a parathyroid hormone for preparing a composition used for reducing the risk of bone fracture in a subject in need thereof.

58. The use of a parathyroid hormone in the manufacture of a medicament for increasing toughness or stiffness of bone at a site of potential or
30 actual trauma.

59. The use of a parathyroid hormone for preparing a composition used for increasing toughness or stiffness of bone at a site of potential or actual trauma.